

PSYCHIATRIC SUMMARY XXII

Summer 2017

By Frederick Langheim, MD, PhD

This issue marks the twenty-second installment consolidating recent clinical updates, mental health policy news, popular press news patients may be reading, and changes in the landscape of psychiatry in Wisconsin.

OF GENERAL INTEREST

FBI Investigating Universal Health Services:

Reported at BuzzFeed (Adams and Lewis [LINK](#)) multiple agencies are investigating the nation's largest chain of psychiatric hospitals, Universal Health Services (UHS), for systematically keeping patients hospitalized longer than necessary (as long as their insurer agrees to pay for) regardless of medical need. This allegation was raised by two nurses, according to three sources with direct knowledge of the investigation.

Ohio Attorney General Sues 5 Drug Makers:

As reported in the AMA Morning Rounds 6/1/2017:

The [Wall Street Journal](#) (5/31, A1, Whalen, Subscription Publication) reports that Ohio Attorney General Mike DeWine filed a lawsuit against five drug makers, claiming they contributed to the opioid epidemic by misrepresenting the risk of addiction from their pain medications. Defendants include Purdue Pharma LP, Endo Health Solutions, Janssen Pharmaceuticals, Cephalon and Allergan PLC.

The [New York Times](#) (5/31, Pérez-Peña, Subscription Publication) reports DeWine "sued the drug makers in a case similar to one that was filed by Mississippi in 2015 and is still pending." Other states and localities have pursued similar options. For example, "West Virginia went after major drug distributors and has reached settlements that will pay the state tens of millions of dollars," while "the City of Chicago, and counties in New York, California and West Virginia, have all started litigation."

The [AP](#) (5/31, Smyth) reports that DeWine is seeking "an injunction stopping the companies from their alleged misconduct and damages for money the state spent on opiates sold and marketed in Ohio." He also "wants customers repaid for unnecessary opiate prescriptions for chronic pain."

CLINICAL PSYCHIATRY IN THE NEWS, IN BRIEF

New TD Treatment(s):

As reported by Linda Johnson in the AP (4/12/17, [LINK](#)) the FDA approved Ingrezza, developed by Neurocrine Biosciences, for treating adult patients with tardive dyskinesia. They are expected to also provide approval in late August for another new treatment created by Israel's Teva Pharmaceuticals.

Post ER Suicide Prevention:

In a multicenter study of post emergency room suicide prevention, Miller et al. (JAMA Psychiatry, [LINK](#)) studied 1376 ER patients with recent suicide attempts or ideation. They compared treatment as usual, with an intervention combining secondary suicide risk screening by the ER physician, discharge resources, and post-ED telephone calls focused on reducing suicide risk. They found that the intervention resulted in a 5% absolute decrease in the proportion of patients subsequently attempting suicide, as well as a 30% reduction in the total number of suicide attempts over a 52-week follow-up period.

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Oxytocin Plus Naltrexone in Autism Treatment:

Published on-line ahead of print at PNAS (Dal Monte et al., [LINK](#)) and publicized by Yale News (Hathaway, [LINK](#)) researchers explored a supralinear improvement in social attention when coupling oxytocin treatment with naltrexone.

Amantadine Adjunct to Antipsychotics:

In a meta-analysis of five RCTs, authors Wei Zheng et al. (Journal of Clinical Psychopharmacology, [LINK](#)) published the following results:

Five RCTs (n = 265) with double-blinded design lasting 8.2 ± 5.9 weeks were included in the analysis. Amantadine outperformed placebo regarding weight reduction with moderate effect size (trials, 3; n = 205; WMD -2.22 kg; P = 0.001, I² = 45%). Amantadine also outperformed placebo at endpoint in the negative symptom (the Positive and Negative Syndrome Scale [PANSS] [1 trial] and the Scale for the Assessment of Negative Symptoms [1 trial]) scores (trials, 2; n = 84; SMD, -0.56; P = 0.01, I² = 12%), but not in the PANSS total scores (trials, 2) (SMD, -0.31; P = 0.16, I² = 0%) and the positive symptom (PANSS [1 trial] and the Scale for the Assessment of Positive Symptoms [1 trial]) scores (SMD, 0.13; P = 0.54, I² = 0%). Except for insomnia (P = 0.007; number needed to harm, 6; 95% confidence interval, 4–16), all-cause discontinuation (risk ratio, 1.12; P = 0.54, I² = 0%) and other adverse events were similar between the amantadine and placebo groups.

Early Trauma and Amygdala Functional Connectivity:

Published in Frontiers in Systems Neuroscience ([LINK](#)), using resting state fMRI, Cisler examined functional connectivity (FC) between medial prefrontal cortex (mPFC) and amygdala in 30 healthy female control subjects and 26 females exposed to physical or sexual assault. “Using a priori ROI, the predicted finding of lessor FC between mPFC and amygdala as a function of early life trauma was replicated in this sample. By contrast, early life trauma was associated with greater large-scale network modularity.”

Deutetrabenazine Approved for Tardive Dyskinesia:

The FDA approved deutetrabenazine (Austedo) for treatment of TD in addition to previous approval for Huntington’s Chorea ([LINK](#) to RCT).

Lung Cancer and Suicide Risk:

Reported at MDLinx (Murphy, [LINK](#)), the suicide rate in cancer is 60% higher than in the general population, while the suicide rate among those with lung cancer is 420% higher.

Antidepressant Use Cognitive Decline:

In a community based cohort study of 7381 individuals 65 years and older, 4% were taking antidepressants (Carrière et al., BMC Med, [LINK](#)). Compared to non-users, tricyclic antidepressant users had lower baseline performances in verbal fluency, visual memory and psychomotor speed, and selective serotonin reuptake inhibitor users in verbal fluency and psychomotor speed. For the two other cognitive abilities, executive function and global cognition, no significant differences were found at baseline irrespective of the antidepressant class. Regarding changes over time, no significant differences were observed in comparison with non-users whatever the cognitive domain, except for a slight additional improvement over the follow-up in verbal fluency skills for tricyclic antidepressant users.

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Assault → Suicidal Ideation:

In a widely publicized article appearing in the Journal of Urban Health, Devylder et al., ([LINK](#)) conducted a population-based survey in four cities of 1615 individuals with police-public encounters. They found that:

Police victimization was associated with suicide attempts but not suicidal ideation in adjusted analyses. Specifically, odds of attempts were greatly increased for respondents reporting assaultive forms of victimization, including physical victimization (odds ratio = 4.5), physical victimization with a weapon (odds ratio = 10.7), and sexual victimization (odds ratio = 10.2). Assessing for police victimization and other violence exposures may be a useful component of suicide risk screening in urban US settings. Further, community-based efforts should be made to reduce the prevalence of exposure to police victimization

Alcohol Use → Hippocampal Atrophy:

Topiwala et al., (British Medical Journal, [LINK](#)) sought to investigate whether moderate alcohol use had a protective or detrimental effect on the human brain. Studying 550 men and women enrolled in the Whitehall study in the UK, they analyzed brain imaging data regarding hippocampal atrophy, grey matter density and white matter microstructure, correlated with the CAGE screening questionnaire. They found:

Higher alcohol consumption over the 30 year follow-up was associated with increased odds of hippocampal atrophy in a dose dependent fashion. While those consuming over 30 units a week were at the highest risk compared with abstainers (odds ratio 5.8, 95% confidence interval 1.8 to 18.6; $P \leq 0.001$), even those drinking moderately (14-21 units/week) had three times the odds of right sided hippocampal atrophy (3.4, 1.4 to 8.1; $P = 0.007$). There was no protective effect of light drinking (1-7 units/week) over abstinence. Higher alcohol use was also associated with differences in corpus callosum microstructure and faster decline in lexical fluency. No association was found with cross sectional cognitive performance or longitudinal changes in semantic fluency or word recall.

Lithium in Pregnancy and Ebstein's Anomaly:

Published in the New England Journal of Medicine ([LINK](#)), Paterno et al. conducted a cohort study involving 1,325,563 pregnancies in women who were enrolled in Medicaid and who delivered a live-born infant between 2000 and 2010. They examined the likelihood of cardiac malformation among infants exposed to lithium in the first trimester to those not exposed to lithium but to lamotrigine. They reported:

Cardiac malformations were present in 16 of the 663 infants exposed to lithium (2.41%), 15,251 of the 1,322,955 nonexposed infants (1.15%), and 27 of the 1945 infants exposed to lamotrigine (1.39%). The adjusted risk ratio for cardiac malformations among infants exposed to lithium as compared with unexposed infants was 1.65 (95% confidence interval [CI], 1.02 to 2.68). The risk ratio was 1.11 (95% CI, 0.46 to 2.64) for a daily dose of 600 mg or less, 1.60 (95% CI, 0.67 to 3.80) for 601 to 900 mg, and 3.22 (95% CI, 1.47 to 7.02) for more than 900 mg. The prevalence of right ventricular outflow tract obstruction defects was 0.60% among lithium-exposed infants versus 0.18% among unexposed infants (adjusted risk ratio, 2.66; 95% CI, 1.00 to 7.06). Results were similar when lamotrigine-exposed infants were used as the reference group.

The authors concluded that:

Maternal use of lithium during the first trimester was associated with an increased risk of cardiac malformations, including Ebstein's anomaly; the magnitude of this effect was smaller than had been previously postulated.

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ECT Reduces Readmission Rates:

In an effort to provide population based statistics to bolster the case for ECT as its availability shrinks across the nation, Slade et al (JAMA Psychiatry, [LINK](#)) conducted a “quasi-experimental instrumental variables probit model of the association correlation of ECT administration with patient risk of 30-day readmission” using data from US general hospitals in 9 states. They reported:

Overall, 2486 of the 162 691 inpatients (1.5%) underwent ECT during their index admission. Compared with other inpatients, those who received ECT were older (mean [SD], 56.8 [16.5] vs 45.9 [16.5] years; $P < .001$) and more likely to be female (65.0% vs 54.2%; $P < .001$) and white non-Hispanic (85.3% vs 62.1%; $P < .001$), have MDD diagnoses (63.8% vs 32.0%; $P < .001$) rather than bipolar disorder (29.0% vs 40.0%; $P < .001$) or schizoaffective disorder (7.1% vs 28.0%; $P < .001$), have a comorbid medical condition (31.3% vs 26.6%; $P < .001$), have private (39.4% vs 21.7%; $P < .001$) or Medicare (49.2% vs 39.4%; $P < .001$) insurance coverage, and be located in urban small hospitals (31.2% vs 22.3%; $P < .001$) or nonurban hospitals (9.0% vs 7.6%; $P = .02$). Administration of ECT was associated with a reduced 30-day readmission risk among psychiatric inpatients with severe affective disorders from an estimated 12.3% among individuals not administered ECT to 6.6% among individuals administered ECT (risk ratio [RR], 0.54; 95% CI, 0.28-0.81). Significantly larger associations with ECT on readmission risk were found for men compared with women (RR, 0.44; 95% CI, 0.20-0.69 vs 0.58; 95% CI, 0.30-0.88) and for individuals with bipolar disorder (RR, 0.42; 95% CI, 0.17-0.69) and schizoaffective disorder (RR, 0.44; 95% CI, 0.11-0.79) compared with those who had MDD (RR, 0.53; 95% CI, 0.26-0.81).

MENTAL HEALTH IN THE POPULAR PRESS

Psychedelics Expand Consciousness (Peer Reviewed):

Picked up throughout the popular press, Schartner et al. published an MEG study exploring measures of various states of consciousness in the journal Nature ([LINK](#)). Using measures of complexity of network connectivity under anesthesia, at rest, and with various forms of psychedelic substances (Psilocybin, LSD, ketamine) Researchers found that brain state complexity was greater under the influence of psychedelics than at normal resting state, while at its lowest level of complexity during propofol anesthesia. They concluded:

These findings suggest that the sustained occurrence of psychedelic phenomenology constitutes an elevated level of consciousness - as measured by neural signal diversity.

Marijuana Treatment for Autism?

Continuing the above trend of illicit substances on conscious state, USA Today (Schwartz, 4/25/2017, [LINK](#)) published a piece regarding ongoing research in Israel exploring the treatment of severe autism using cannabidiol. This work developed from incidental findings in an earlier study of cannabidiol treatment of epilepsy wherein researchers noted improvement in autistic behaviors among those being treated for epilepsy.

Prenatal SSRI ≠ Autism:

Also widely reported in the popular press, simultaneously appearing JAMA articles which appear to put to rest any concern that SSRI use during pregnancy may be associated with autism. One, a retrospective cohort study of 35,906 singleton births by Brown et al. ([LINK](#)) found no statistically significant association between exposure to serotonergic antidepressants and Autism “compared with no exposure in inverse probability of treatment-weighted analyses or when comparing exposed with unexposed siblings.” The other, Sujan et al. ([LINK](#)) also a retrospective cohort study, this time of 1,580,629 Swedish offspring, adjusting for confounds, concluded that:

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First-trimester antidepressant exposure was significantly associated with preterm birth (odds ratio, 1.3 in a sibling comparison analysis) but not with risk of being born small for gestational age or later autism spectrum disorder or attention-deficit/hyperactivity disorder.

Stimulants = Fewer MVAs in ADHD:

Picked up by Reuters and appearing in JAMA Psychiatry, Chang et al., ([LINK](#)) explored the relationship between stimulant use and motor-vehicle accidents (you may recall an earlier Scandinavian study also looking at violent and criminal behavior [LINK](#)). In this recent study, the authors looked at a cohort of over 2.3 million individuals with ADHD, comparing risk for motor-vehicle accidents while on stimulants and off. They reported that:

In the within-individual analyses, male patients with ADHD had a 38% (odds ratio, 0.62; 95% CI, 0.56-0.67) lower risk of MVCs in months when receiving ADHD medication compared with months when not receiving medication, and female patients had a 42% (odds ratio, 0.58; 95% CI, 0.53-0.62) lower risk of MVCs in months when receiving ADHD medication. Similar reductions were found across all age groups, across multiple sensitivity analyses, and when considering the long-term association between ADHD medication use and MVCs. Estimates of the population-attributable fraction suggested that up to 22.1% of the MVCs in patients with ADHD could have been avoided if they had received medication during the entire follow-up.

Safe as Psilocybins?

The AMA Morning Rounds of 5/24 ran the following:

[USA Today](#) (5/24, Bowerman) reports that psilocybin hallucinogenic mushrooms are the safest recreational drug, according to the annual Global Drug Survey. According to USA Today, “only .2% of almost 10,000 people who reported taking psilocybin hallucinogenic mushrooms in 2016 reported that they needed emergency medical treatment.” Rates of emergency medical treatment “for MDMA, LSD, alcohol and cocaine were almost five times higher.”

According to [CNBC](#) (5/24, Graham), the report explains that the mushrooms may be safer “because of intrinsic safety of magic mushrooms (the greatest risk is picking the wrong type), the smaller dosing using units (a single mushroom versus an LSD tab) and a greater understanding of how many mushrooms may constitute a typical dose for a desired effect.”

Exercise To Prevent Peripartum Depression:

Published in Birth Issues in Perinatal Care, Poyatos-León et al., ([LINK](#)) conducted a meta-analysis including twelve studies regarding exercise and mental health during pregnancy and the postpartum period. They reported:

Effect size for the relationship between physical activity interventions during pregnancy and the postpartum period on postpartum depressive symptoms was 0.41 (95% CI 0.28-0.54). Heterogeneity was $I^2 = 33.1\%$ ($P = .117$). When subgroup analyses were done, pooled effect sizes were 0.67 (95% CI 0.44-0.90) for mothers who met postpartum depressive symptoms criteria at baseline based on specific scales, and 0.29 (95% CI 0.14-0.45) for mothers who did not meet those depressive symptoms criteria at baseline.

Extra Virgin Olive Oil to Prevent AD?

Appearing in Annals of Clinical and Translational Neurology, Lauretti, Iuliano, and Praticò explored how consumption of extra virgin olive oil (EVOO), a major component of the Mediterranean diet, has been associated with reduced incidence of Alzheimer's disease (AD). They reported:

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Triple transgenic mice (3xTg) received either regular chow or a chow diet supplemented with EVOO starting at 6 months of age for 6 months, then assessed for the effect of the diet on the AD-like neuropathology and behavioral changes. Compared with controls, mice receiving the EVOO-rich diet had an amelioration of their behavioral deficits, and a significant increase in the steady state levels of synaptophysin, a protein marker of synaptic integrity. In addition, they had a significant reduction in insoluble A β peptide levels and deposition, lower amount of phosphorylated tau protein at specific epitopes, which were secondary to an activation of cell autophagy.